UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,216	01/04/2002	E. Antonio Chiocca	0609.5050005/JAG/KRM/FRC	3452

26111 7590 07/13/2006

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/035,216	**Applicant(s)** CHIOCCA ET AL.	
	Examiner Daniel M. Sullivan	**Art Unit** 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 June 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Daniel M Sullivan, Ph.D.
Primary Examiner
Art Unit: 1636

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 40-45 and 47-56 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* (1998) *Genome Res.* 8:404-412 in view of Wang *et al.* (1996) *J. Virol.* 70:8422-8430 as evidenced by Woodfield *et al.* (2000) *Nucl. Acids Res.* 28:3323-3331 for the reasons of record and herein below in the response to Applicant arguments.

Claims 40, 56 and 57 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* (*supra*) in view of Wang *et al.* (*supra*) and further in view of Saeki *et al.* (1998) *Hum. Gene Ther.* 9:2787-2794 for the reasons of record herein below in the response to Applicant arguments.

Response to Arguments

In response to the *prima facie* rejection and arguments of record, Applicant first contends that, even if one were motivated to combine the teachings of Kim et al. and Wang et al., the method of the instant claims would not have been obvious because the skilled artisan would be able to achieve the improved efficiency of transduction of mammalian cells without recombining a BAC with an amplicon vector. Applicant asserts that, in view of the teachings of Kim et al. and Wang et al., the skilled artisan would have inserted the genomic insert of Kim (containing the GFP, *neo* and *lac*Z genes) into the amplicon vector of Wang et al. using the molecular cloning techniques that were used to create the amplicon vector taught therein. Applicant urges, "There is nothing in either Kim or Wang that would have suggested *recombining* the entire BAC of Kim with the amplicon of Wang." (Page 8, final sentence.)

These arguments have been fully considered but are not deemed persuasive. It is first noted that Applicant's remarks suggest that there is a distinction between "recombining" as recited in the instant claims and "insertion of DNA using standard restriction enzyme and ligation reactions". However, the instant specification states in paragraph 0097, "Although site-specific recombination is preferred, any other type of recombination known to those skilled in the art may be used as well, including homologous recombination or ligation." (Emphasis added.) Thus, standard restriction enzyme and ligation reactions are within the broadest reasonable construction of the claims in light of the specification. Furthermore, contrary to Applicant's assertion, recombining the entire BAC with the amplicon is suggested by the teachings of Kim et al., which concern converting BAC's comprising human genomic DNA to vectors suitable for transformation of mammalian cells by retrofitting BAC vectors with elements that enable their propagation in mammalian cells. (See the discussion bridging pp. 8-9 of the Office Action mailed 9 August 2005 and Figure 1 of Kim et al.) Kim et al. is the primary reference used in the rejection and is relied upon to teach the method. Wang et al. is relied upon only to teach the elements of an HSV-based amplicon and the efficient delivery of genes using HSV-based amplicons. There is nothing of record to indicate that the skilled artisan would not have been motivated to use the method of retrofitting BAC vectors as taught by Kim et al. and there is clearly no teaching in the art of record to suggest that the skilled artisan should exclude the BAC vector when producing an amplicon as suggested by the cited art.

Applicant further argues, "having already subjected the BAC of Kim to one round of recombination, a person of ordinary skill in the art would have been precluded from subjecting

the resulting 'retrofitted BAC clone' to *another* round of recombination since there would be no available recombination sites...In addition the amplicon of Wang lacks a recombination site. Thus, simply combining the 'teachings' of Kim and Wang would not result in a process that falls within the scope of the currently pending claims." (Page 9, ¶ 1.)

These arguments have been fully considered but are not deemed persuasive because they are based on a misconception of the rejection. As stated in making the *prima facie* case, "The method of Kim *et al.* comprises recombining a large capacity cloning vector comprising a genomic DNA insert with a vector comprising the elements that enable selection of the vector in mammalian cells (see especially the paragraph bridging pages 410-411)" (page 8, ¶4), "Wang *et al.* teaches a hybrid herpesvirus amplicon vector comprising herpesvirus cleavage/packaging sequence and a herpesvirus origin of replication (see especially the first full paragraph on page 8423, Figure 1 and the caption thereto), which is demonstrated to provide highly efficient delivery of DNA into a wide range of human cells (see especially Table 2). Wang *et al.* further teaches that the large insert capacity of HSV-based amplicon vectors 'offers the possibility to carry large DNA fragments including regulatory genomic elements, (paragraph bridging the left and right columns on page 8422)" (page 9, ¶2), and, "It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of retrofitting a BAC clone of Kim *et al.* to insert the HSV-amplicon vector taught by Wang *et al.* to produce an HSV-based amplicon vector comprising said genomic DNA insert according to the method of the instant claims" (page 10, ¶1). The modification referred to in the Office Action is clearly the substitution of an HSV-based amplicon for the marker gene construct taught by Kim et al. not the addition of an amplicon vector to the already retrofitted BAC clone of Kim et al. Furthermore, Applicant's statement that the BAC clone no longer comprises a recombination site after a first round of recombination is not accurate. Kim et al. is using standard loxP sites for the recombination reaction and the skilled artisan would be aware that the product of Cre mediated insertion via standard loxP sites is a nucleic acid comprising two functional loxP sites flanking the inserted DNA, as clearly illustrated in Figure 1 of Kim et al. Finally, the failure of Wang et al. to teach an amplicon vector comprising a recombination site does not render the claimed invention non-obvious over the art considered as a whole because Wang et al. is not relied upon to teach retrofitting a BAC vector by recombination. The teachings of Kim et al., and the generally high level of skill in the art, provide all that is necessary to retrofit a DNA a BAC clone by site-specific recombination, including inserting a recombination site into an HSV amplicon to be used in retrofitting a BAC clone according to the method of Kim et al.

Thus, for the reasons set forth in the previous Office Actions and herein above, the claims stand rejected under 35 USC §103(a) as obvious over the art.